REMARKS/ARGUMENTS

Claims 1-26 remain in this application. Claims 9, 12 and 14 are currently amended. Claim 11 is original. Claims 1-8 and 15-26 remain withdrawn. Claims 10 and 13 have been canceled without prejudice.

Claim rejections under 35 USC 112.

The Examiner has rejected Claims 9-11 and 13-14 because of the alleged vagueness of the terminology "a therapeutically effective amount" in claim 9. Amended claim 9 now includes the limitation "an amount of a statin drug therapeutically effective for reducing the incidence of atrial fibrillation in the mammal". The Applicant respectfully submits that the scope of the therapeutically effective amount is now clear as both the condition to treat and the subject experiencing the condition are defined in the amended claim 9. The exact amount to use would depend on the mammal and substances involved. However, the Applicant respectfully submits that the person skilled in the art would be able to determine easily given a specific mammal whether or not a given amount of the substance used in the claimed invention is therapeutically effective or not by performing simple well-known experiments without undue experimentation.

The Examiner has rejected claim 12 for failure to indicate from which claim it depends. This mistake has been corrected.

The Examiner has rejected claims 9-14 because, according to the Examiner, the specification is enabling for treating dogs with atrial fibrillation with a statin, but does not provide enablement for preventing AF with a wide variation of statins.

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First, the Applicant respectfully disagrees with the Examiner regarding the scope of the disclosure as the specification **does not disclose how to treat dogs** with statins but **how to prevent**, or **at least reduce the incidence** of atrial fibrillation. For example, the application as filed states in the first paragraph of page 13:

> Figure 3 shows the progression of mean AF duration in dogs subjected to atrial tachycardia in the presence of each of the interventions studied. With vitamin C (panel A), vitamins C and E (panel B) and sustained-release vitamin C (panel C), progressive increases in AF duration to means between ~400 to 600 seconds occurred by day 7, not significantly different from ATP-only dogs. In contrast, atrial tachycardia-induced AF promotion was virtually abolished in simvastatin-treated dogs (panel D).

Therefore, the Applicant respectfully submits that any argument presented by the Examiner in relation to treatment of atrial fibrillation and any documents cited to that effect are not applicable to the present invention as no claim to such treatment is made.

Furthermore, the Examiner cites documents according to which not all atrial fibrillation is preventable. Amended claim 9 is now directed to the reduction of the incidence of atrial fibrillation. Therefore, this claim no longer has a limitation to the effect of a total elimination of atrial fibrillation.

Yet furthermore, the Applicant respectfully submits that from the discussion, and more specifically from the first paragraph of page 16 of the application as filed, a reader skilled in the art would be led to understand that while only Simvastatin was used in the experiments described in the application, all statins have similar modes of actions on many systems and would be effective similarly to Simvastatin in

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preventing AF:

Potential Underlying Mechanisms

Statins act as antioxidants by inhibiting superoxide production,[29] as well as by increasing nitric oxide bioavailability.[30,31] Simvastatin increases catalase and glutathione peroxidase activity.[32] Thus, without wishing to be bound by any particular hypothesis, it would appear that simvastatin's efficacy is due to an antagonism of oxidant pathways involved in atrial tachycardia remodeling.[10] The antioxidant properties of both vitamin C and E are well-recognized,[33,34] however, the ability of exogenous vitamin C and E to increase the body's already substantial stores of these important endogenous antioxidants may be insufficient to significantly alter atrial antioxidant capacity. An alternative explanation lies in the anti-inflammatory properties of statins[14,15] in the context of the potential role of inflammation in AF.[12,13] Although CRP concentrations were measured in the dogs used in the experiments described above, no significant changes with ATP or simvastatin administration were observed.

In view of the above, the Applicant respectfully submits that claims 9, 11-12 and 14 are now clear and unambiguous and in accordance with 35 USC 112 and that they are fully supported by the disclosure. Accordingly, withdrawal of the rejections of claims 9, 11-12 and 14 is respectfully requested.

Claim rejections under 35 USC 102 and 35 USC 103.

The Examiner has rejected claims 9-10 and 13-14 under 35 USC 102 as being anticipated by West et al. (2002, J. Hypertension, 20:2513-2517). The Examiner states that the reference teaches administering a statin to a patient with atrial

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fibrillation. The Examiner also combines West with US Patent 6,376,242, hereinafter Hanson, and US Patent 6,235,311, hereinafter Ullah. The Examiner states that Hanson teaches administering a statin to a human suffering from atrial fibrillation and that Ullah teaches administering a statin to reduce the risk of cardiovascular event, including coronary artery disease.

Amended claim 9 reads as follows:
"A method **of reducing the incidence of atrial fibrillation** (AF) by substrate modification comprising the step of administering to a mammal in need thereof an amount of a statin drug therapeutically effective for reducing the incidence of atrial fibrillation in the mammal." (Emphasis added)

Amended claim 9 is directed to the prevention of atrial fibrillation, and not to the treatment of atrial fibrillation. The Applicant respectfully submits that there is absolutely no indication in West or Hanson that administering a statin can **prevent** atrial fibrillation. Also, if statin is administered to a patient that already has atrial fibrillation, as stated by the Examiner, atrial fibrillation **was not prevented**, as claimed in claim 9, which is in total contradiction with the claimed invention. Finally, while Ullah discusses the prevention of coronary heart disease, atrial fibrillation is a problem of the heart muscle **in which the atrium contracts erratically. Atrial fibrillation is not a coronary heart disease**, such diseases being related to **blood vessels surrounding the heart**. Accordingly, the applicant respectfully submits that the above-emphasized limitation of claim 9 is neither taught nor suggested by any of the references cited by the Examiner.

Claims 11-12 and 14 depend directly or indirectly on claim 9. As such, they include all the limitations of this base claim, including the above-discussed limitations. Accordingly, the Applicant respectfully submits that claims 11-12 and 14 are neither taught nor suggested by West, Hanson and Ullah, either taken alone or in

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combination.

Respectfully submitted,

Louis Tessier, Reg 45 289
Agent for the Applicant
60 Balfour
Mount-Royal, QC, H3P 1L6
CANADA

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